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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,282	04/19/2006	Rainer Papp	13111-00038-US1	1949

30678 7590 03/26/2010

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EXAMINER	
NOLAN, JASON MICHAEL	
ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
03/26/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,282	PAPP ET AL.	
	Examiner	Art Unit	
	JASON M. NOLAN	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-8,10-14 and 16-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-8,10-14 and 16-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment – After Non-Final Rejection, filed November 30, 2009. As filed, Claims 2-8, 10-14, & 16-22 are pending; of which, Claims 11-13, 21, & 22 are currently amended. Claims 1, 9, & 15 are cancelled.

Response to Amendment

Applicant's amendments with respect to Claims 11-13, 21, & 22 have been fully considered and are entered. The amendments to independent Claims 13, 21, & 22 clarify the definition and scope of the term "phosphoramidite." The instant claims, as amended, now include a structure for the phosphoramidite compounds (formulae I & II). The fact that formulae I and II may be overinclusive with respect to the chemical dictionary definitions of "phosphoramidite" provided in the previous Office Action is now irrelevant because the presentation of said formulae in the claims establishes a clear scope to the term.

Claims 21 & 22 are drawn to a hydroformylation process, wherein the catalyst-complex utilizes a ligand defined as a compound according to formulae I or II. The instant specification states that the purpose of using a ligand defined as a compound according to formulae I or II is to provide stability to the catalyst-complex because it is known in the art that catalysts degrade over time in a hydroformylation process (p. 5, ll. 6-22). Claim 13 is drawn to a method of stabilizing a catalyst-complex in a hydroformylation process via the use of a ligand defined as a compound according to

formulae I or II. The Examiner concludes that independent Claims 13 & 21 define the same invention in different language. It is noted that Applicants have a right to define the invention per their choosing; however, any prior art that is relevant to Claim 13 or 21 is equally relevant to the other. Claim 22 is drawn to the same inventive concept as Claims 13 & 21; however, Claim 22 limits the choice of base to those immobilized on a solid phase.

Response to Arguments

Applicant's arguments have been fully considered. The Examiner concludes that the arguments are persuasive in part and non-persuasive in part. First, Applicants assert that the Bunel *et al.* reference (US 6,229,052; "the '052 patent") discloses a catalytic system (metal and ligand), wherein the metal complex is attached to a solid support. The instant application recites a limitation wherein the base is attached to a solid-support. The Examiner has reconsidered the '052 patent and agrees with Applicant in this difference. For this reason, the instant Office Action is Non-Final.

Applicants note that Ahlers *et al.* (WO02/083695 & US 7,173,138) does not suggest the use of a base in the hydroformylation process. Applicants note that Dennis *et al.* (US 4,567,306; "the '306 patent") does not suggest utilizing a phosphoramidite ligand on a rhodium catalyst. Applicants assert that one of ordinary skill in the art "would have no reason to believe that adding triethylamine to the structurally different complex catalysts in Ahlers would provide the same benefits as the addition of the cyclic

phosphate ligands of Dennis, especially because the pnicogen chelate complexes in Ahlers already contain basic groups bound to the metal complex."

The Examiner notes that it is a difficult legal exercise to establish what a hypothetical skilled artisan would have reason to *believe*. However, the exercise becomes less difficult when considering what said hypothetical skilled artisan would or would not *know*, considering the state of the prior art as a whole. A fair reading of the '306 patent suggests that one of ordinary skill in the art would *know* that tertiary amines have been used in hydroformylation processes for the purpose of, *inter alia*, increasing catalytic stability. The '306 patent does not purport to limit this suggestion to a particular catalytic system, but fairly suggests that adding a tertiary amine, specifically triethylamine, would be useful in to provide stability in a hydroformylation processes generally. As such, one of ordinary skill in the art would have been aware of this at the time the instant invention was conceived. Therefore, Applicant's argument is unpersuasive and the obviousness rejection is maintained herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Obviousness under 35 U.S.C. § 103 is a question of law, but is based on underlying facts of each case. The Supreme Court stated that an invention may be found obvious if it would have been obvious to a person having ordinary skill to try a course of conduct:

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

KSR International Co. v. Teleflex Inc., 550 U.S. 398, 421 (2007).

Although a combination of relevant options in a particular art may be obvious to try, there are instances where an invention would not have been obvious to try:

1) When the inventor would have had to try all possibilities in a field unreduced by direction of the prior art. In other words, when "what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is

likely to be successful" an invention would not have been obvious. *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). This is another way to express the *KSR* prong requiring the field of search to be among a "finite number of identified" solutions. 550 U.S. at 421.

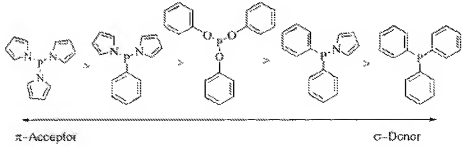
2) An invention is not obvious to try where vague prior art does not guide an inventor toward a particular solution. A finding of obviousness would not obtain where "what was 'obvious to try' was to explore a technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." *O'Farrell*, 853 F.2d at 903. This expresses the same idea as the *KSR* requirement that the identified solutions be "predictable." 550 U.S. at 421.

In the instant application, Claims 13 & 14 are drawn to a method of stabilizing a catalytically active fluid in a hydroformylation reaction and Claims 2-8, 10-12, & 16-22 are drawn to a hydroformylation process in the presence of said catalytically active fluid. In both scenarios, a base is utilized. In both scenarios, the same inventive concept (stabilizing the catalyst with particular ligands and utilizing a base) is used in the same context (hydroformylation). Claim 22 limits the base to solid-supported bases.

The inventive concept relates to a hydroformylation process using a metal complex having a 1-pyrrole-phosphorus ligand according to the formulae I and II, wherein the process is conducted in the presence of a base. Hydroformylation is a well known and important process; the instant application is drawn to an improvement thereof, wherein the alleged improvement achieves high hydroformylation activity and good yields of desired product (instant specification, p. 1).

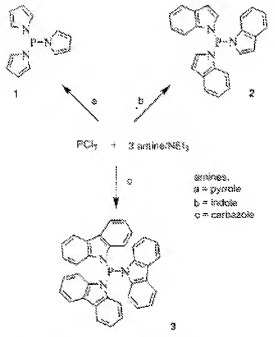
Claims 2-8, 10-14, & 16-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jackstell *et al.* (*Eur. J. Org. Chem.* 2001, 3871-3877; "Jackstell") in view of Ahlers *et al.* (WO02/083695 & US 7,173,138; "the '138 patent"), US 5,731,472 ("the '472 patent"); US 4,567,306 ("the '306 patent", IDS); US 4,260,828; US 4,283,562; van Leeuwen in Chapter 9 of Catalysis by Metal Complexes, Vol. 22, Rhodium Catalyzed Hydroformylation, 2002, Kluwer Acad. Pub., pp. 233-251; Moloy *et al. J. Am. Chem. Soc.* 1995, *117*, 7696-7710; Trzeciak *et al. J. Chem. Soc. Dalton Trans.*, 1997, 1831-1837 (IDS); and Xu *et al. Tetrahedron Lett.* 1997, *38(42)*, 7337-7340.

1. Determining the scope and contents of the prior art – Jackstell discloses that the catalytic hydroformylation of olefins (or "oxo process") is an old (discovered in 1938; p. 3871) and well known synthetic transformation, which is widely used in industry (more than 6.6 million tons of product produced with this process (p. 3871). Jackstell discloses that there are limitations in a continuous hydroformylation process because of limited stability of some catalytic ligands, such as phosphite ligands. *Id.* Jackstell then states that "phosphanes would offer advantages over phosphites in terms of stability." *Id.* Jackstell then discusses the properties of phosphorus ligands on p. 3872, shown below.

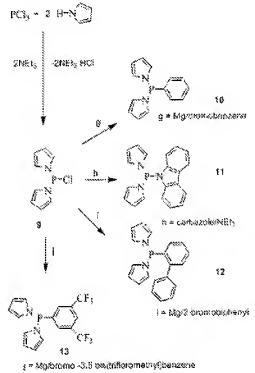


Scheme 2. π-Acceptor and σ-donor properties of different P ligands

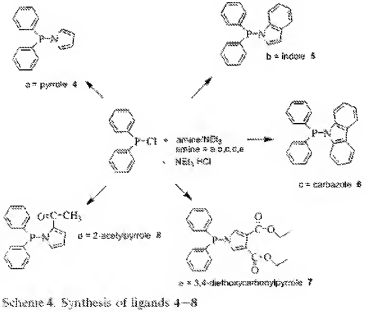
Jackstell then discloses the synthesis of various phosphorus ligands, shown below, and hydroformylation experiments utilizing said ligands. *See*, pp. 3872-3877.



Scheme 3. Synthesis of ligands 1–3



Scheme 5. Synthesis of ligands 10–13



Scheme 4. Synthesis of ligands 4–8

Several of the phosphorus ligands disclosed by Jackstell fall within the scope of formula I, wherein R^1 = a pyrrole group bound by the nitrogen atom to the phosphorus atom; a = b= 0; and R^2 = aryl or heteroaryl.

It is noted that Jackstell was not the first to synthesize 1-pyrrolylphosphorus ligands (they have been studied since at least 1995; *See* Moloy *et al.*). It is also noted that Jackstell was not the first to use 1-pyrrolylphosphorus ligands in the catalytic hydroformylation process (they have been used since at least 1997; *See* Trzeciak *et al.*).

The '138 patent discloses a hydroformylation process in the presence of a catalyst that utilizes 1-pyrrolylphosphorus ligands (*See* Claims 9, 10, & 17, shown below) having a bridging group Q (Q = Y in the instant application; *See* structure in Claims 1 & 9 in the '138 patent). Claims 13-21 and Examples 1-37 (specification, col. 47-55) outline the synthesis, use, and stability of the phosphoramidite ligands. The '138 patent discloses work-up procedures, including fractionalization, in col. 32-41.

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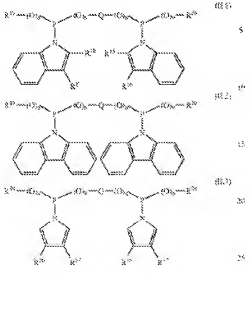

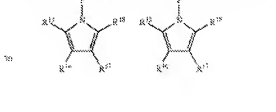

Jackstell discloses that the stability of the catalyst in the hydroformylation process is a pressing concern. The '472 patent states, "stabilization of the catalyst and organophosphite ligand remains a primary concern of the art. Obviously catalyst stability is a key issue in the employment of any catalyst. Loss of catalytic activity due to undesirable reactions of the highly expensive rhodium catalysts can be detrimental to the production of the desired aldehyde. . . " *See* col. 1-2. *See also*, van Leeuwen at 233 ("catalyst stability has been a key issue, next to selectivity and activity.").

The use of a base is one means to stabilizing a hydroformylation catalyst-complex. The '472 patent discloses the use of "free heterocyclic nitrogen compounds . . . to prevent and/or lessen deactivation of metal-organopolyphosphite ligand complex catalysts that may occur over the course of time during processes, e.g., a hydroformylation process . . ." *See*, col. 2, ll. 50-54. The '306 patent discloses the use of tertiary amines (particularly triethylamine; col. 4, ll. 65-68) in hydroformylation media to increase stability. *See*, col. 3-6. The '306 patent demonstrates that better results are observed with the use of a tertiary amine in a comparison study of hydroformylation reactions with and without triethylamine (*See* Tables 1 & II).

At the time of invention, the use of solid-supported bases (or polymer-supported base) in organic synthesis were known in the art. Xu *et al.* discloses general method for the use of a polymer supported guanidine base.

2. Ascertaining the differences between the prior art and the claims at issue – Jackstell and the '138 patent do not disclose the use of a base in their hydroformylation experiments.

3. Resolving the level of ordinary skill in the pertinent art – the level of ordinary skill in the art may be found by inquiring into: (1) the type of problems encountered in the art; (2) prior art solutions to those problems; (3) the rapidity with which innovations are made; (4) the sophistication of the technology; and (5) the education level of active workers in the field. *Custom Accessories, Inc.*, 807 F.2d at 962. All of those factors may not be present in every case, and one or more of them may predominate. *Envtl. Designs, Ltd. v. Union Oil Co.*, 713 F.2d 693, 696 (Fed.Cir.1983).

Based on the typical education level of active workers in the field of synthetic organic chemistry, as well as the high degree of sophistication required to solve problems encountered in the art, the Examiner finds that a person of ordinary skill in the art would have at least a college degree in the field of organic chemistry and at least four years of work experience, i.e. a masters or doctorate level scientist.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness – as pointed out on p. 5 (ll. 9-19) of the instant specification, the addition of a base provides additional stability to the hydroformylation catalyst and such stability is surprising because the ligands already contain basic nitrogen atoms. Applicants have provided studies of hydroformylation reactions comparing the results with and without the use of a base.

However, Applicant's finding that the use of a base improves the stability of the catalyst-ligand system and the overall result is not an unexpected finding. As pointed out above, the prior art has long recognized stability of the catalyst-complex as one of the primary concerns in continuous hydroformylation reactions. *See, i.e.*, US 4,260,828

and 4,283,562. The use of a base, in particular, to enhance stabilization has been recognized in the art. *See, i.e.*, US 4,567,306 and 5,731,472.

Conclusion – the Federal Circuit stated "[o]bviousness does not require absolute predictability of success . . . all that is required is a reasonable expectation of success." *O'Farrell* at 903-904. *In the instant case*, the prior art cited above supports the conclusion that a person of ordinary skill in the art, at the time of invention, would have been motivated to try known options within their technical grasp in the hydroformylation process art.

Jackstell and the '138 patent are the starting point, which disclose hydroformylation processes which utilize a catalyst-complex containing 1-pyrrolylphosphorus ligands. This starting point is not vague, but in fact the references disclose specific catalytic complexes that are likely to be successful in hydroformylation chemistry. Those references and the secondary references disclose that one of the major concerns in hydroformylation chemistry is the stabilization of the catalyst-complex. The secondary references disclose that utilizing a base to improve stabilization was known in the art at the time of invention. Further, the use of solid-supported bases in organic synthesis was known in the art at the time of invention.

Thus, the prior art as a whole discloses a finite number of predictable solutions for a skilled artisan attempting to solve the identified problem. Because the specification fails to produce evidence of unexpected results, a long-felt industrial need, or other secondary considerations, the Examiner concludes that one of ordinary skill in

the art would have been motivated to arrive at the instant claimed invention with an expectation of success.

Conclusion

No claims are allowed.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jason M. Nolan whose telephone number is (571) 272-4356 and e-mail is Jason.Nolan@uspto.gov. The examiner can normally be reached Monday - Friday (9:00AM - 5:30PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M^{c}Kane, may be contacted at Joseph.McKane@uspto.gov or (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system, (Private PAIR or Public PAIR). Status information for unpublished applications is available through Private PAIR only. For information about the PAIR system, see http://pair-direct.uspto.gov. For questions on Private PAIR system, contact the Electronic Business Center at (866) 217-9197.

/Jason M. Nolan/

Examiner, Art Unit 1626